Access DB# 76906

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: GARY COUNTS Examiner #: 78696 Date: 10-1-02
Art Unit: 1641 Phone Number 305-1444 Serial Number: 09/992,174
Mail Box and Bldg/Room Location: 7D16 (CM1) Results Format Preferred (circle): PAPER DISK E-MAIL
7E12
If more than one search is submitted, please prioritize searches in order of need. 1ST)
****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Method for diagnosing multiple sclerosis and an Assay therefore

Inventors (please provide full names): Mario Moscarello

Andrea Chamczuk

Earliest Priority Filing Date: 11-14-2001

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please Search Attached Claim 22.

POINT OF CONTACT:
PAUL SCHULWITZ
TECHNICAL INFO. SPECIALIST
CM1 6B06 TEL. (703) 305-1954

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	NA Sequence (#)		STN	225.40
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 10/2	Bibliographic		Dr.Link	
Date Completed: 10/2	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 30	Fulltext	X	Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 59	Other		Other (specify)	

PTO-1590 (8-01)

Claim 22(NEW). A method for diagnosing or monitoring multiple sclerosis (MS) in a mammal comprising:

obtaining a sample of body fluid from said mammal, wherein said body fluid includes blood, blood products and saliva;

performing an enzyme-linked immunosorbent assay (ELISA) effective to bind myelin basic protein (MBP) and characterized by utilizing heparin sulphate bound to non-specific binding sites on MBP, thereby providing an assay whose specificity is due to binding of serum antibodies to specific binding sites on MBP;

determining a level of at least one autoantibody selected from the group consisting of anti-MBP IgG, anti-MBP IgM or a mixture thereof specific for said at least one protein in said sample; and,

comparing said level of said at least one autoantibody with statistically significant levels thereof, whereby a diagnosis or monitoring of MS in said mammal is made.

FILE 'HCAPLUS' ENTERED AT 14:38:09 ON 02 OCT 2002
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FILE COVERS 1907 - 2 Oct 2002 VOL 137 ISS 14
FILE LAST UPDATED: 1 Oct 2002 (20021001/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> d que l19
L4          5923 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MULTIPLE SCLEROSIS/CT
L5          9117 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "IMMUNOASSAY (L) ENZYME-LINKED
                  IMMUNOSORBENT ASSAY"+OLD/CT
L6          3285 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MYELIN BASIC PROTEIN+OLD/CT
L8             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "HEPARIN SULFATE"/CN
L9         19413 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8
L10         8920 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ANTIBODIES (L) AUTOANTIBODIES
                 "+OLD/CT
L11         1002 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "IMMUNOGLOBULINS (L) AUTOANTIB
                 ODIES, G"+OLD/CT
L12          410 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "IMMUNOGLOBULINS (L) AUTOANTIB
                 ODIES, M"+OLD/CT
L19            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND (L8 OR L9) AND ((L10
                 OR L11 OR L12) OR L5 OR L6)


=> d que l21
L4          5923 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MULTIPLE SCLEROSIS/CT
L5          9117 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "IMMUNOASSAY (L) ENZYME-LINKED
                  IMMUNOSORBENT ASSAY"+OLD/CT
L6          3285 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MYELIN BASIC PROTEIN+OLD/CT
L8             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "HEPARIN SULFATE"/CN
L9         19413 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8
L10         8920 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "ANTIBODIES (L) AUTOANTIBODIES
                 "+OLD/CT
L11         1002 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "IMMUNOGLOBULINS (L) AUTOANTIB
                 ODIES, G"+OLD/CT
L12          410 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "IMMUNOGLOBULINS (L) AUTOANTIB
```

```
               ODIES, M"+OLD/CT
L20          41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND L5
L21          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND (L6 OR (L8 OR L9) OR
               (L10 OR L11 OR L12))


=> s l19 or l21
L86          15 L19 OR L21

=> b medline
FILE 'MEDLINE' ENTERED AT 14:38:38 ON 02 OCT 2002

 FILE LAST UPDATED: 1 OCT 2002 (20021001/UP).  FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary.  Enter HELP THESAURUS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> d que l31
L22       20619 SEA FILE=MEDLINE ABB=ON  PLU=ON  MULTIPLE SCLEROSIS+NT/CT
L23       59749 SEA FILE=MEDLINE ABB=ON  PLU=ON  ENZYME-LINKED IMMUNOSORBENT
                ASSAY/CT
L24        5321 SEA FILE=MEDLINE ABB=ON  PLU=ON  MYELIN BASIC PROTEINS+NT/CT
L25       52569 SEA FILE=MEDLINE ABB=ON  PLU=ON  AUTOANTIBODIES+NT/CT
L26       78499 SEA FILE=MEDLINE ABB=ON  PLU=ON  IMMUNOGLOBULIN G+NT/CT
L27       37969 SEA FILE=MEDLINE ABB=ON  PLU=ON  IMMUNOGLOBULIN M+NT/CT
L29         265 SEA FILE=MEDLINE ABB=ON  PLU=ON  L22 AND L23
L30          30 SEA FILE=MEDLINE ABB=ON  PLU=ON  L29 AND L24
L31          16 SEA FILE=MEDLINE ABB=ON  PLU=ON  L30 AND ((L25 OR L26 OR L27))


=> d que l38
L22       20619 SEA FILE=MEDLINE ABB=ON  PLU=ON  MULTIPLE SCLEROSIS+NT/CT
L23       59749 SEA FILE=MEDLINE ABB=ON  PLU=ON  ENZYME-LINKED IMMUNOSORBENT
                ASSAY/CT
L25       52569 SEA FILE=MEDLINE ABB=ON  PLU=ON  AUTOANTIBODIES+NT/CT
L26       78499 SEA FILE=MEDLINE ABB=ON  PLU=ON  IMMUNOGLOBULIN G+NT/CT
L27       37969 SEA FILE=MEDLINE ABB=ON  PLU=ON  IMMUNOGLOBULIN M+NT/CT
L36        1159 SEA FILE=MEDLINE ABB=ON  PLU=ON  L22 AND (L26 OR L27)
L37         101 SEA FILE=MEDLINE ABB=ON  PLU=ON  L36 AND L25
L38          13 SEA FILE=MEDLINE ABB=ON  PLU=ON  L37 AND L23


=> s l31 or l38
L87          27 L31 OR L38

=> s l31 and l38
L88           2 L31 AND L38

=> b embase
FILE 'EMBASE' ENTERED AT 14:39:54 ON 02 OCT 2002
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 FILE COVERS 1974 TO 26 Sep 2002 (20020926/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l48
L39       19555 SEA FILE=EMBASE ABB=ON  PLU=ON  "MULTIPLE SCLEROSIS"/CT
L40       50230 SEA FILE=EMBASE ABB=ON  PLU=ON  "ENZYME LINKED IMMUNOSORBENT
                ASSAY"/CT
L42       50451 SEA FILE=EMBASE ABB=ON  PLU=ON  HEPARIN/CT
L47         287 SEA FILE=EMBASE ABB=ON  PLU=ON  L39 AND L40
L48           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L47 AND L42


=> d que l51
L39       19555 SEA FILE=EMBASE ABB=ON  PLU=ON  "MULTIPLE SCLEROSIS"/CT
L41        3578 SEA FILE=EMBASE ABB=ON  PLU=ON  "MYELIN BASIC PROTEIN"/CT
L43       17757 SEA FILE=EMBASE ABB=ON  PLU=ON  AUTOANTIBODY/CT
L44       43743 SEA FILE=EMBASE ABB=ON  PLU=ON  "IMMUNOGLOBULIN G"/CT
L45       23106 SEA FILE=EMBASE ABB=ON  PLU=ON  "IMMUNOGLOBULIN M"/CT
L49         891 SEA FILE=EMBASE ABB=ON  PLU=ON  L39 AND (L44 OR L45)
L50          43 SEA FILE=EMBASE ABB=ON  PLU=ON  L49 AND L43
L51          13 SEA FILE=EMBASE ABB=ON  PLU=ON  L50 AND L41


=> d que l52
L39       19555 SEA FILE=EMBASE ABB=ON  PLU=ON  "MULTIPLE SCLEROSIS"/CT
L40       50230 SEA FILE=EMBASE ABB=ON  PLU=ON  "ENZYME LINKED IMMUNOSORBENT
                ASSAY"/CT
L41        3578 SEA FILE=EMBASE ABB=ON  PLU=ON  "MYELIN BASIC PROTEIN"/CT
L42       50451 SEA FILE=EMBASE ABB=ON  PLU=ON  HEPARIN/CT
L43       17757 SEA FILE=EMBASE ABB=ON  PLU=ON  AUTOANTIBODY/CT
L44       43743 SEA FILE=EMBASE ABB=ON  PLU=ON  "IMMUNOGLOBULIN G"/CT
L45       23106 SEA FILE=EMBASE ABB=ON  PLU=ON  "IMMUNOGLOBULIN M"/CT
L52           5 SEA FILE=EMBASE ABB=ON  PLU=ON  L39 AND L40 AND L41 AND (L42
                OR L43 OR L44 OR L45)


=> s l48 or l51 or l52
L89          17 L48 OR L51 OR L52

=> b drugu
FILE 'DRUGU' ENTERED AT 14:40:29 ON 02 OCT 2002
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FILE LAST UPDATED: 30 SEP 2002      <20020930/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<
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```
=> d que l60
L53       27900 SEA FILE=DRUGU ABB=ON  PLU=ON  MS OR MULTIPLE SCLEROSIS
L54        6050 SEA FILE=DRUGU ABB=ON  PLU=ON  ELISA OR ENZYME LINKED IMMUNOSOR
                BENT ASSAY
L55         887 SEA FILE=DRUGU ABB=ON  PLU=ON  MBP OR MYELIN BASIC PROTEIN
L59         134 SEA FILE=DRUGU ABB=ON  PLU=ON  L53 AND L54
L60           2 SEA FILE=DRUGU ABB=ON  PLU=ON  L59 AND L55


=> d que l64
L53       27900 SEA FILE=DRUGU ABB=ON  PLU=ON  MS OR MULTIPLE SCLEROSIS
L54        6050 SEA FILE=DRUGU ABB=ON  PLU=ON  ELISA OR ENZYME LINKED IMMUNOSOR
                BENT ASSAY
L56       20564 SEA FILE=DRUGU ABB=ON  PLU=ON  HEPARIN
L64           3 SEA FILE=DRUGU ABB=ON  PLU=ON  L53 AND L54 AND L56


=> d que l68
L53       27900 SEA FILE=DRUGU ABB=ON  PLU=ON  MS OR MULTIPLE SCLEROSIS
L54        6050 SEA FILE=DRUGU ABB=ON  PLU=ON  ELISA OR ENZYME LINKED IMMUNOSOR
                BENT ASSAY
L57        1751 SEA FILE=DRUGU ABB=ON  PLU=ON  AUTOANTIBOD?
L68           1 SEA FILE=DRUGU ABB=ON  PLU=ON  L53 AND L54 AND L57


=> d que l71
L53       27900 SEA FILE=DRUGU ABB=ON  PLU=ON  MS OR MULTIPLE SCLEROSIS
L54        6050 SEA FILE=DRUGU ABB=ON  PLU=ON  ELISA OR ENZYME LINKED IMMUNOSOR
                BENT ASSAY
L56       20564 SEA FILE=DRUGU ABB=ON  PLU=ON  HEPARIN
L58       13452 SEA FILE=DRUGU ABB=ON  PLU=ON  IGG OR IMMUNOGLOBULIN(W)(G OR
                M) OR IGM
L71           1 SEA FILE=DRUGU ABB=ON  PLU=ON  L53 AND L54 AND L56 AND L58


=> s l60 or l64 or l68 or l71
L90           6 L60 OR L64 OR L68 OR L71

=> b wpix
FILE 'WPIX' ENTERED AT 14:41:10 ON 02 OCT 2002
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FILE LAST UPDATED: 01 OCT 2002              <20021001/UP>
MOST RECENT DERWENT UPDATE           200263   <200263/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> SLART (Simultaneous Left and Right Truncation) is now
    available in the /ABEX field. An additional search field
    /BIX is also provided which comprises both /BI and /ABEX <<<

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<
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>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d que l85
L72       13217 SEA FILE=WPIX ABB=ON  PLU=ON  MS OR MULTIPLE SCLEROSIS
L73        2861 SEA FILE=WPIX ABB=ON  PLU=ON  ELISA OR ENZYME LINKED IMMUNOSORB
                ENT ASSAY
L74         441 SEA FILE=WPIX ABB=ON  PLU=ON  MBP OR MYELIN BASIC PROTEIN
L76         498 SEA FILE=WPIX ABB=ON  PLU=ON  AUTO ANTIBOD? OR AUTOANTIBOD?
L77        3370 SEA FILE=WPIX ABB=ON  PLU=ON  IGG OR IMMUNOGLOBULIN(W)(G OR M)
                OR IGM
L85           1 SEA FILE=WPIX ABB=ON  PLU=ON  L72 AND L73 AND L74 AND (L76 OR
                L77)


=> dup rem l86 l88 l89 l90 l85
FILE 'HCAPLUS' ENTERED AT 14:41:32 ON 02 OCT 2002
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FILE 'MEDLINE' ENTERED AT 14:41:32 ON 02 OCT 2002

FILE 'EMBASE' ENTERED AT 14:41:32 ON 02 OCT 2002
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FILE 'DRUGU' ENTERED AT 14:41:32 ON 02 OCT 2002
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FILE 'WPIX' ENTERED AT 14:41:32 ON 02 OCT 2002
COPYRIGHT (C) 2002 THOMSON DERWENT
PROCESSING COMPLETED FOR L86
PROCESSING COMPLETED FOR L88
PROCESSING COMPLETED FOR L89
PROCESSING COMPLETED FOR L90
PROCESSING COMPLETED FOR L85
L91           39 DUP REM L86 L88 L89 L90 L85 (2 DUPLICATES REMOVED)

=> d l91 bib ab hitind 1-39

L91  ANSWER 1 OF 39  HCAPLUS  COPYRIGHT 2002 ACS
AN   2002:90341  HCAPLUS
DN   136:133595
TI   Identifying antigen clusters for monitoring a global state of an immune
     system
IN   Cohen, Irun R.; Domany, Eytan; Quintana, Fransisco J.; Hed, Guy; Getz, Gad
PA   Yeda Research and Development Co. Ltd., Israel
SO   PCT Int. Appl., 78 pp.
     CODEN: PIXXD2
```

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002008755	A2	20020131	WO 2001-IL660	20010718

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI IL 2000-137460 A 20000724

AB A method is provided for the clustering and identifying predefined antigens that are reactive with serum autoantibodies derived from patients in need of diagnosis of disease or monitoring of treatment. A coupled two-way clustering algorithm is used to identify the specific antigens in a cluster of antigens that are involved in antibody binding.

IC ICM G01N033-53
CC 15-1 (Immunochemistry)
Section cross-reference(s): 14

IT **Antibodies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**autoantibodies**; method for identifying antigens and autoantigens involved in autoimmune disorders and other diseases in humans)

IT **Immunoassay**
(**enzyme-linked immunosorbent assay**; method for identifying antigens and autoantigens involved in autoimmune disorders and other diseases in humans)

IT Algorithm
Autoimmune disease
Blood analysis
Cartilage
Celiac disease
Disease, animal
Graves' disease
Human
Immune system
Immunity
Immunodeficiency
Infection
Inflammation
Injury
Mental disorder
Multiple sclerosis
Myasthenia gravis
Neoplasm
Peptide library
Poisoning, biological
Psoriasis
Rheumatoid arthritis
Sjogren's syndrome
Transplant and Transplantation

Vitiligo
(method for identifying antigens and autoantigens involved in autoimmune disorders and other diseases in humans)

IT Actins
Annexins
Carbohydrates, biological studies
Cardiolipins
Cholinergic receptors
Collagens, biological studies
Cytokines
Fatty acids, biological studies
Fetuins
Fibrinogens
Fibronectins
Histones
Immunoglobulins
Interleukin 10
Interleukin 2
Interleukin 4
Laminins
Myelin basic protein
Myosins
Nucleic acids
Peptides, biological studies
Proteins
Spectrins
Thyroglobulin
Transferrins
Tropomyosins
Tubulins
Vimentins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for identifying antigens and autoantigens involved in autoimmune disorders and other diseases in humans)

IT 57-88-5, Cholesterol, biological studies 70-18-8, Glutathione, biological studies 1071-23-4, Phosphoethanolamine 9001-05-2, Catalase 9001-12-1, Collagenase 9001-25-6, Blood-coagulation factor VII 9001-26-7, Factor II 9001-78-9, Alkaline phosphatase 9001-99-4, Ribonuclease 9002-10-2, Tyrosinase 9003-99-0, Peroxidase **9005-49-6**, Heparin, biological studies 9014-08-8, Enolase 9024-52-6, Aldolase 9034-51-9, Hemoglobin a 9035-51-2, Cytochrome p450, biological studies 24937-83-5, Poly a 25086-81-1, Poly t 25191-14-4, Poly g 30811-80-4, Poly c 39324-30-6, Pepstatin 80295-32-5, Complement C1 80295-33-6, Complement C1q 80295-59-6, Complement c9 85305-87-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for identifying antigens and autoantigens involved in autoimmune disorders and other diseases in humans)

L91 ANSWER 2 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002032877 EMBASE
TI Occupational exposures and autoimmune diseases.
AU Cooper G.S.; Miller F.W.; Germolec D.R.
CS D.R. Germolec, Environmental Immunology Laboratory, Natl. Inst. of Environ. Health Sci., 111 Alexander Dr., Research Triangle Park, NC 27709, United States
SO International Immunopharmacology, (2002) 2/2-3 (303-313).

Refs: 103
ISSN: 1567-5769 CODEN: IINMBA
PUI S 1567-5769(01)00181-3
CY Netherlands
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
035 Occupational Health and Industrial Medicine
052 Toxicology
LA English
SL English
AB Autoimmune diseases are pathologic conditions defined by abnormal autoimmune responses and characterized by immune system reactivity in the form of autoantibodies and T cell responses to self-structures. Here we review the limited but growing epidemiologic and experimental literature pertaining to the association between autoimmune diseases and occupational exposure to silica, solvents, pesticides, and ultraviolet radiation. The strongest associations (i.e., relative risks of 3.0 and higher) have been documented in investigations of silica dust and rheumatoid arthritis, lupus, scleroderma and glomerulonephritis. Weaker associations are seen, however, for solvent exposures (in scleroderma, undifferentiated connective tissue disease, and multiple sclerosis) and for farming or pesticide exposures (in rheumatoid arthritis). Experimental studies suggest two different effects of these exposures: an enhanced proinflammatory (TH1) response (e.g., TNF-.alpha. and IL-1 cytokine production with T cell activation), and increased apoptosis of lymphocytes leading to exposure to or modification of endogenous proteins and subsequent autoantibody formation. The former is a general mechanism that may be relevant across a spectrum of autoimmune diseases, whereas the latter may be a mechanism more specific to particular diseases (e.g., ultraviolet radiation, Ro autoantibodies, and lupus). Occupational exposures are important risk factors for some autoimmune diseases, but improved exposure assessment methods and better coordination between experimental/animal models and epidemiologic studies are needed to define these risks more precisely.
CT Medical Descriptors:
*occupational exposure
*autoimmune disease
disease association
Graves disease
Hashimoto disease
multiple sclerosis
myasthenia gravis
rheumatoid arthritis
systemic lupus erythematosus
systemic sclerosis
polymyositis
scleroderma
Th1 cell
cytokine production
antibody production
apoptosis
risk factor
human
nonhuman
review
priority journal

Drug Descriptors:
***autoantibody: EC, endogenous compound**
*silicon dioxide: TO, drug toxicity
*solvent: TO, drug toxicity
*pesticide: TO, drug toxicity
*cytokine: EC, endogenous compound
interleukin 1: EC, endogenous compound
tumor necrosis factor alpha: EC, endogenous compound
thyrotropin: EC, endogenous compound
thyroglobulin: EC, endogenous compound
glutamate decarboxylase: EC, endogenous compound
myelin basic protein: EC, endogenous compound
cholinergic receptor: EC, endogenous compound
immunoglobulin G: EC, endogenous compound
rheumatoid factor: EC, endogenous compound
DNA topoisomerase: EC, endogenous compound
laminin: EC, endogenous compound
amino acid transfer RNA ligase: EC, endogenous compound
vinyl chloride: TO, drug toxicity
trichloroethylene: TO, drug toxicity
thinner: TO, drug toxicity
xylene: TO, drug toxicity
paint: TO, drug toxicity
hexachlorobenzene: TO, drug toxicity

RN (silicon dioxide) 10279-57-9, 14464-46-1, 14808-60-7, 15468-32-3, 60676-86-0, 7631-86-9; (thyrotropin) 9002-71-5; (thyroglobulin) 9010-34-8; (glutamate decarboxylase) 9024-58-2; (immunoglobulin G) 97794-27-9; (rheumatoid factor) 9009-79-4; (DNA topoisomerase) 80449-01-0; (laminin) 2408-79-9; (amino acid transfer RNA ligase) 9028-02-8; (vinyl chloride) 75-01-4; (trichloroethylene) 79-01-6; (xylene) 1330-20-7; (hexachlorobenzene) 118-74-1, 55600-34-5

L91 ANSWER 3 OF 39 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
AN 2002:324694 HCAPLUS
DN 137:59773
TI A rapid ELISA-based serum assay for myelin basic protein in multiple sclerosis
AU Chamczuk, A. J.; Ursell, M.; O'Connor, P.; Jackowski, G.; Moscarello, M. A.
CS Structural Biology and Biochemistry, The Hospital For Sick Children, Research Institute, Toronto, ON, M5G 1X8, Can.
SO Journal of Immunological Methods (2002), 262(1-2), 21-27
CODEN: JIMMBG; ISSN: 0022-1759
PB Elsevier Science B.V.
DT Journal
LA English
AB We have developed a sensitive, ELISA-based assay to detect autoantibodies to myelin basic protein (MBP) in human serum. Autoantibody levels were measured in 98 normal healthy adults (age range 20-66) and 94 clin. definite multiple sclerosis (MS) cases (age range 18-63). Of the MS patients, 77% had elevated levels of MBP autoantibodies (IgG) whereas only five normal individuals had antibody levels increased over normal. From the receiver-operator curve (ROC), the mean.+-.2SD as clin. decision limit offers high sensitivity (77%) and specificity (95%). No change in assay performance was obsd. when Hb, triglycerides or bilirubin were added to serum samples. The success of the assay is dependent on the use of heparin, an anionic mol., which neutralizes the pos. charge on the highly

cationic MBP.
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 14
IT Blood analysis
Blood serum
Human
Multiple sclerosis
Sample preparation
(ELISA-based serum assay for myelin basic protein in multiple sclerosis)
IT **Myelin basic protein**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(ELISA-based serum assay for myelin basic protein in multiple sclerosis)
IT **Antibodies**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**autoantibodies**; ELISA-based serum assay for myelin basic protein in multiple sclerosis)
IT **Immunoassay**
(**enzyme-linked immunosorbent assay**; ELISA-based serum assay for myelin basic protein in multiple sclerosis)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 4 OF 39 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
AN 2001:868803 HCAPLUS
DN 135:370658
TI Modulation of T-cell receptor interactions
IN Rhode, Peter; Wittman, Vaughan; Weidanz, Jon A.; Burkhardt, Martin; Card, Kimberlyn F.; Tal, Rony; Acevedo, Jorge; Wong, Hing C.
PA Sunol Molecular Corporation, USA
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001090747	A2	20011129	WO 2001-US15699	20010516
WO 2001090747	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-206920P P 20000525
AB Disclosed are methods for identifying compds. that modulate the interaction between T cell receptors (TCR) and major histocompatibility complex (MHC) antigens. The invention has many useful applications including providing high throughput screening assays for detecting compns. that can modulate an immune response.

IC ICM G01N033-48
CC 15-10 (Immunochemistry)
IT **Immunoassay**
(**enzyme-linked immunosorbent assay**; methods for identifying compds. that modulate the interaction between T cell receptors and major histocompatibility complex antigens)
IT Cell adhesion
Cell proliferation
Chemiluminescent substances
Colorimetric indicators
DNA formation
Electric potential
Electrolytes
Fluorescent substances
Immunotherapy
Luminescent substances
Multiple sclerosis
Phosphorescent substances
RNA formation
Solvents
Test kits
(methods for identifying compds. that modulate the interaction between T cell receptors and major histocompatibility complex antigens in relation to)
IT CD3 (antigen)
Myelin basic protein
Polymers, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods for identifying compds. that modulate the interaction between T cell receptors and major histocompatibility complex antigens in relation to)

L91 ANSWER 5 OF 39 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 2001-15067 DRUGU P
TI Effective antigen-specific immunotherapy in the marmoset model of **multiple sclerosis**.
AU McFarland H I; Lobito A A; Johnson M M; Palardy G R; Yee C S K; Jordan E K; Frank J A; Tresser N; Genain C P; Lenardo M J
CS Nat.Inst.Allergy-Infect.Dis.Bethesda; Nat.Inst.Health-Bethesda; Nat.Inst.Neurological-Dis.Stroke-Bethesda; Univ.California; Alexion
LO Bethesda, Md., San Francisco, Cal.; New Haven, Conn., USA
SO J.Immunol. (166, No. 3, 2116-21, 2001) 4 Fig. 3 Tab. 43 Ref.
CODEN: JOIMA3 ISSN: 0022-1767
AV Lab. Immunology, Nat. Inst. Allergy Infectious Dis., Nat. Inst. Health, Building 10, Room 11N311, 10 Center Drive, Bethesda, MD 20892-1892, U.S.A. (12 authors). (M.J.L.). (e-mail: mlenardo@nih.gov).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB I.v. MP-4 prevented the clinical symptoms of experimental allergic encephalomyelitis (EAE) and delayed white matter disease evident on MRI in marmosets. High-dose MP-4 treatment was associated with less lymphocyte infiltration in the CNS, and decreased T cell proliferative responses and **myelin basic protein** (**MBP**)-specific Ab production. The mRNA levels of IL-4 and IL-10

were lower than the levels of IFN-gamma or TGF-beta after incubation with MP-4. Results suggest that the choice of Ag for immunomodulation may be critical for successful treatment and provide new hope for Ag-specific therapy in humans.

L91 ANSWER 6 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001389487 EMBASE
TI Autoimmune diseases: A spectrum of disease processes.
AU Ogedegbe H.O.
CS Dr. H.O. Ogedegbe, Department of Environmental Health, Molecular and Clinical Sciences, Florida Gulf Coast University, Fort Myers, FL, United States
SO Laboratory Medicine, (2001) 32/11 (670-679).
Refs: 37
ISSN: 0007-5027 CODEN: LBMEBX
CY United States
DT Journal; General Review
FS 005 General Pathology and Pathological Anatomy
006 Internal Medicine
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LA English
SL English
AB Autoimmune diseases may either be organ specific or non-organ specific and are caused by the failure of the immune system to recognize self-antigens and thus react against self. The mechanisms of the disease processes include interaction of antibodies with cell surface components, formation of autoantigen-autoantibody complexes and sensitization of T cells. Common features of autoimmune diseases are the breakdown of tolerance of self-antigens and the modification of autoantigens during apoptosis which leads to the development of autoantibodies by bypassing the normal tolerance mechanisms. Because the autoimmune diseases share many clinical findings, making a differential diagnosis is often challenging and usually the causes cannot be determined.
CT Medical Descriptors:
*autoimmune disease: DI, diagnosis
*autoimmune disease: DT, drug therapy
*autoimmune disease: ET, etiology
*autoimmunity
Hashimoto disease: DI, diagnosis
Hashimoto disease: ET, etiology
Graves disease: DI, diagnosis
Graves disease: DT, drug therapy
Graves disease: ET, etiology
insulin dependent diabetes mellitus: DI, diagnosis
insulin dependent diabetes mellitus: ET, etiology
atrophic gastritis: DI, diagnosis
atrophic gastritis: ET, etiology
Addison disease: DI, diagnosis
Addison disease: ET, etiology
Goodpasture syndrome: DI, diagnosis
Goodpasture syndrome: ET, etiology
myasthenia gravis: DI, diagnosis
myasthenia gravis: DT, drug therapy
myasthenia gravis: ET, etiology
systemic lupus erythematosus: DI, diagnosis

systemic lupus erythematosus: ET, etiology
rheumatoid arthritis: DI, diagnosis
rheumatoid arthritis: ET, etiology
Sjoegren syndrome: DI, diagnosis
Sjoegren syndrome: ET, etiology
progressive systemic sclerosis: DI, diagnosis
progressive systemic sclerosis: ET, etiology
chronic liver disease: DI, diagnosis
chronic liver disease: ET, etiology
primary biliary cirrhosis: DI, diagnosis
primary biliary cirrhosis: ET, etiology
multiple sclerosis: DI, diagnosis
multiple sclerosis: ET, etiology
autoimmune hemolytic anemia: DI, diagnosis
autoimmune hemolytic anemia: ET, etiology
bullous skin disease: DI, diagnosis
bullous skin disease: ET, etiology
human
review
Drug Descriptors:
*autoantigen
***autoantibody**
*HLA antigen
*major histocompatibility antigen class 1
*major histocompatibility antigen class 2
*cytokine
CD4 antigen
interleukin 1beta
interleukin 12
Fas antigen
FAS ligand
HLA DR antigen
HLA DQ antigen
basement membrane antibody
antinuclear antibody
tumor necrosis factor alpha
lymphotoxin
rheumatoid factor
gamma interferon: EC, endogenous compound
interleukin 2: EC, endogenous compound
glucocorticoid: EC, endogenous compound
mineralocorticoid: EC, endogenous compound
cyanocobalamin
transforming growth factor beta: EC, endogenous compound
platelet derived growth factor: EC, endogenous compound
myelin basic protein
HLA B antigen
immunoglobulin G
complement component C3
complement component C4
immunoglobulin M
nitric oxide: EC, endogenous compound
cholinesterase inhibitor: DT, drug therapy
antithyroid agent: DT, drug therapy
RN (interleukin 12) 138415-13-1; (rheumatoid factor) 9009-79-4; (gamma interferon) 82115-62-6; (interleukin 2) 85898-30-2; (cyanocobalamin) 53570-76-6, 68-19-9, 8064-09-3; (immunoglobulin G) 97794-27-9; (complement

component C3) 80295-41-6; (complement component C4) 80295-48-3, 80295-71-2; (immunoglobulin M) 9007-85-6; (nitric oxide) 10102-43-9

L91 ANSWER 7 OF 39 MEDLINE
AN 2001108741 MEDLINE
DN 21065710 PubMed ID: 11137588
TI An IgM anti-MBP Ab in a case of Waldenstrom's macroglobulinemia with polyneuropathy expressing an idiotype reactive with an MBP epitope immunodominant in MS and EAE.
AU Noerager B D; Inuzuka T; Kira J; Blalock J E; Whitaker J N; Galin F S
CS Department of Physiology and Biophysics, University of Alabama at Birmingham, Birmingham, AL 35294, USA.
NC AI37670 (NIAID)
NS29719 (NINDS)
SO JOURNAL OF NEUROIMMUNOLOGY, (2001 Feb 1) 113 (1) 163-9.
Journal code: 8109498. ISSN: 0165-5728.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208
AB In a previously described case of Waldenstrom's Macroglobulinemia, complicated by polyneuropathy, the IgM/lambda monoclonal antibody (mAb) was highly reactive with myelin basic protein (MBP). Given our demonstration that V lambda x, a recently described murine lambda variable region gene product, can itself bind MBP as well as confer MBP reactivity to an Ab, the possibility of a shared idiotypy between murine V lambda x and this human IgM/lambda anti-MBP was investigated. We characterized the epitope specificity of the macroglobulinemia patient's MBP-reactive IgM/lambda using indirect ELISA procedures with MBP, a citrullinated isomer of MBP termed C8, or peptide fragments of MBP as the coating antigens and monospecific Ab to V lambda x as the secondary Ab. The patient's MBP-reactive IgM/lambda was recognized by Ab specific for V lambda x and, like murine mAb containing V lambda x bound human MBP but not MBP-C8 nor other common autoantigens such as DNA, thyroglobulin, or actin. The anti-MBP reactivity was selective for MBP peptide 90-170 and preferentially recognized MBP peptide 84-96. Thus, the patient's macroglobulin and perhaps certain other human Ab with a 'V lambda x idiotype' bind to MBP peptide residues 84-96, an immunodominant peptide in multiple sclerosis patients. Such binding may be involved in the pathogenesis of neural damage in patients with neuroimmunologic disorders related to plasma cell dyscrasias or autoimmunity.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Autoantibodies: BL, blood
*Encephalomyelitis, Experimental Autoimmune: IM, immunology
Enzyme-Linked Immunosorbent Assay
*Immunodominant Epitopes: IM, immunology
***Immunoglobulin M: BL, blood**
Macroglobulins: IM, immunology
***Multiple Sclerosis: IM, immunology**
***Myelin Basic Proteins: IM, immunology**
Peptide Fragments: IM, immunology
*Polyneuropathies: IM, immunology

Rabbits
*Waldenstrom Macroglobulinemia: IM, immunology
CN 0 (Autoantibodies); 0 (Immunodominant Epitopes); 0 (Immunoglobulin M); 0 (Macroglobulins); 0 (Myelin Basic Proteins); 0 (Peptide Fragments)

L91 ANSWER 8 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002021025 EMBASE
TI Primary progressive multiple sclerosis.
AU Montalban X.; Rio J.
CS X. Montalban, Clinical Neuroimmunology Unit, Vall d'Hebron University Hospital, Psg Vall d'Hebron 119-129, E-08035 Barcelona, Spain
SO Neurological Sciences, (2001) 22/SUPPL. 2 (S41-S48).
Refs: 74
ISSN: 1590-1874 CODEN: NESCCX
CY Italy
DT Journal; Article
FS 008 Neurology and Neurosurgery
014 Radiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
CT Medical Descriptors:
***multiple sclerosis: DI, diagnosis**
***multiple sclerosis: DT, drug therapy**
***multiple sclerosis: RT, radiotherapy**
disease course
prognosis
genetic association
haplotype
immunoglobulin production
blood brain barrier
relapse
pathology
nuclear magnetic resonance imaging
cerebrospinal fluid analysis
evoked visual response
clinical trial
patient selection
diagnostic accuracy
disease classification
lymph node irradiation
outcomes research
human
article
Drug Descriptors:
HLA antigen: EC, endogenous compound
immunoglobulin G: DT, drug therapy
immunoglobulin G: EC, endogenous compound
immunoglobulin G: IV, intravenous drug administration
autoantibody: EC, endogenous compound
myelin basic protein: EC, endogenous compound
proteolipid protein: EC, endogenous compound
cytokine: EC, endogenous compound
cell adhesion molecule: EC, endogenous compound
cyclophosphamide: DT, drug therapy
azathioprine: DT, drug therapy
salazosulfapyridine: DT, drug therapy

cyclosporin: DT, drug therapy
glatiramer: DT, drug therapy
methotrexate: DT, drug therapy
cladribine: DT, drug therapy
beta interferon: DT, drug therapy
beta interferon: IM, intramuscular drug administration
interferon beta serine: DT, drug therapy
placebo
mitoxantrone: DT, drug therapy
RN (immunoglobulin G) 97794-27-9; (cyclophosphamide) 50-18-0; (azathioprine) 446-86-6; (salazosulfapyridine) 599-79-1; (cyclosporin) 79217-60-0; (glatiramer) 147245-92-9, 28704-27-0; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (cladribine) 4291-63-8; (interferon beta serine) 90598-63-3; (mitoxantrone) 65271-80-9, 70476-82-3

L91 ANSWER 9 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001149754 EMBASE
TI Gene therapy for tolerance and autoimmunity: Soon to be fulfilled promises?.
AU El-Amine M.; Melo M.E.F.; Scott D.W.
CS D.W. Scott, Department of Immunology, American Red Cross, Jerome H. Holland Laboratory, Rockville, MD 20855, United States. scottd@usa.redcross.org
SO Clinical Immunology, (2001) 99/1 (1-6).
Refs: 40
ISSN: 1521-6616 CODEN: CLIIFY
CY United States
DT Journal; (Short Survey)
FS 022 Human Genetics
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
CT Medical Descriptors:
*gene
*autoimmunity
*autoimmune disease: DT, drug therapy
*gene therapy
immunological tolerance
T lymphocyte
B lymphocyte
immunization
multiple sclerosis: DT, drug therapy
rheumatoid arthritis: DT, drug therapy
bone marrow transplantation
systemic lupus erythematosus: ET, etiology
human
nonhuman
clinical trial
short survey
priority journal
Drug Descriptors:
cytokine: DT, drug therapy
cytokine: EC, endogenous compound
autoantigen: EC, endogenous compound
gamma interferon: EC, endogenous compound
epitope: EC, endogenous compound
major histocompatibility antigen class 2: EC, endogenous compound

autoantibody: EC, endogenous compound
vaccine: CT, clinical trial
vaccine: DT, drug therapy
immunoglobulin: EC, endogenous compound
T lymphocyte receptor: EC, endogenous compound
myelin basic protein: EC, endogenous compound
DNA
Fas antigen: EC, endogenous compound
complement component C1q: EC, endogenous compound
complement component C4: EC, endogenous compound
immunoglobulin G: EC, endogenous compound
interphotoreceptor retinoid binding protein: EC, endogenous compound
glutamate decarboxylase: EC, endogenous compound
insulin: EC, endogenous compound
hybrid protein

RN (gamma interferon) 82115-62-6; (immunoglobulin) 9007-83-4; (DNA) 9007-49-2; (complement component C1q) 80295-33-6; (complement component C4) 80295-48-3, 80295-71-2; (immunoglobulin G) 97794-27-9; (glutamate decarboxylase) 9024-58-2; (insulin) 9004-10-8

L91 ANSWER 10 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:368723 HCAPLUS
DN 133:16299
TI Diagnosis of demyelinating or spongiform disease by determining antibodies to myelin or myelin neurofilaments
IN Ebringer, Alan
PA King's College, UK
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000031545	A1	20000602	WO 1999-GB3936	19991125
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 9915695	A	20010814	BR 1999-15695	19991125
	EP 1133696	A1	20010919	EP 1999-956219	19991125
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002530679	T2	20020917	JP 2000-584308	19991125
PRAI	GB 1998-25948	A	19981126		
	WO 1999-GB3936	W	19991125		

AB A method for diagnosing spongiform disease or demyelinating disease in vertebrates, including BSE, MS and CJD, which comprises assaying a biol. sample for antibodies which bind to myelin and/or myelin neurofilaments or to one or more antigenic (immunogenic) parts thereof. An ELISA for detg. IgA autoantibodies in serum samples used bovine myelin or bovine neurofilaments absorbed in wells of microtiter plates and

peroxidase-anti-cow IgA conjugate.
IC ICM G01N033-68
CC 15-1 (Immunochemistry)
Section cross-reference(s): 14
IT **Antibodies**
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(**autoantibodies**; diagnosis of demyelinating or spongiform disease by detg. antibodies to myelin or myelin neurofilaments)
IT Blood analysis
Cattle
Diagnosis
Multiple sclerosis
Test kits
Vertebrate (Vertebrata)
(diagnosis of demyelinating or spongiform disease by detg. antibodies to myelin or myelin neurofilaments)
IT **Immunoassay**
(**enzyme-linked immunosorbent assay**; diagnosis of demyelinating or spongiform disease by detg. antibodies to myelin or myelin neurofilaments)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 11 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:876728 HCAPLUS
DN 134:41103
TI Ig fractions with immunomodulation activity, their isolation from polyvalent i.v. Igs, and their therapeutic use
IN Bourel, Dominique; Bruley-Rosset, Martine; Dhainaut, Frederic; Lirochon, Jacky
PA Laboratoire Francais du Fractionnement et de Biotechnologies, Fr.
SO Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1059088	A1	20001213	EP 2000-401601	20000607
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	FR 2794460	A1	20001208	FR 1999-7153	19990607
	FR 2794461	A1	20001208	FR 1999-16632	19991229
	WO 2000074717	A1	20001214	WO 2000-FR1560	20000607
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	FR 1999-7153	A	19990607		
	FR 1999-16632	A	19991229		

AB The invention provides a process for the isolation of Ig fractions from i.v. polyvalent Igs which will be esp. responsible for the immunomodulatory effect obsd. during the treatment of certain autoimmune diseases. The invention rests on Ig fractions having reactivity with respect to IgM, IgG F(ab')2 or the hapten DNP and little or no reactivity with respect to non-self antigens, i.e. Ig fractions having idiotype interactions (connected fraction) or which comprise natural antibodies reacting with DNP. These fractions show a polyreactivity with respect to given autoantigens.

IC ICM A61K039-395
ICS C07K016-42; C07K016-06; C07K016-18; C07K001-22; A61P037-06

CC 15-3 (Immunochemistry)

IT Actins
Myelin basic protein
Myosins
Tubulins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Ig fractions with immunomodulation activity, isolation from polyvalent i.v. Igs, and therapeutic use)

IT **Antibodies**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**autoantibodies**; Ig fractions with immunomodulation activity, isolation from polyvalent i.v. Igs, and therapeutic use)

IT **Immunoassay**
(**enzyme-linked immunosorbent assay**; Ig fractions with immunomodulation activity, isolation from polyvalent i.v. Igs, and therapeutic use)

IT **Multiple sclerosis**
(therapeutic agents; Ig fractions with immunomodulation activity, isolation from polyvalent i.v. Igs, and therapeutic use)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 12 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:662591 HCAPLUS
DN 133:331661
TI Clinical and analytical evaluation of an enzyme immunoassay for myelin basic protein in cerebrospinal fluid
AU Ohta, Mitsuhiro; Ohta, Kiyoe; Ma, Jie; Takeuchi, Juji; Saida, Takahiko; Nishimura, Masataka; Itoh, Nobuyuki
CS Clinical Research Center, Utano National Hospital, Kyoto, 616-8255, Japan
SO Clinical Chemistry (Washington, D. C.) (2000), 46(9), 1326-1330
CODEN: CLCHAU; ISSN: 0009-9147
PB American Association for Clinical Chemistry
DT Journal
LA English
AB RIA of myelin basic protein (MBP) in cerebrospinal fluid (CSF) is commonly used a biochem. marker of demyelination in patients with multiple sclerosis (MS). Our aim was to develop a sufficiently sensitive ELISA for MBP and evaluate it clin. in patients with MS. The ELISA used anti-bovine MBP antibody coated on plates and biotinylated anti-MBP antibody. The bound antibody complex was quantified with streptavidin-horseradish peroxidase. MBP was detd. in CSF from 84 MS patients and 55 patients other neurol. diseases. The resp. within- and between-assay CVs and 7.2% at 200 ng/L, and 6.3% and 8.8% at 2000 ng/L. The det

was 30 ng/l. Most of the MS patients with acute exacerbations had markedly increased MBP in the CSF. Longitudinal studies of six MS patients with recurrent exacerbation confirmed this observation. MBP concns. from 78 MS patients, as tested with our ELISA, correlated well with those obtained by RIA ($r = 0.9$; $P < 0.01$), but the detection limit of the ELISA was much lower than that of the RIA. This convenient ELISA with higher sensitivity than the existing assays is a suitable routine assay that provides a diagnostic indicator of myelin breakdown in the central nervous system; moreover, it is an excellent indicator of MS disease activity.

CC 9-10 (Biochemical Methods)
Section cross-reference(s): 14

IT Cerebrospinal fluid
Diagnosis
Multiple sclerosis
(clin. and anal. evaluation of enzyme immunoassay for myelin basic protein in cerebrospinal fluid)

IT **Myelin basic protein**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(clin. and anal. evaluation of enzyme immunoassay for myelin basic protein in cerebrospinal fluid)

IT **Immunoassay**
(enzyme-linked immunosorbent assay; clin. and anal. evaluation of enzyme immunoassay for myelin basic protein in cerebrospinal fluid)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 13 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2000240708 EMBASE
TI Intrathecal IgG synthesis and autoantibody-secreting cells in multiple sclerosis.
AU Sellebjerg F.; Jensen C.V.; Christiansen M.
CS F. Sellebjerg, Department of Neurology, University of Copenhagen, Glostrup Hospital, 57 Nordre Ringvej, DK-2600 Glostrup, Copenhagen, Denmark. sellebjerg@dadlnet.dk
SO Journal of Neuroimmunology, (1 Aug 2000) 108/1-2 (207-215).
Refs: 66
ISSN: 0165-5728 CODEN: JNRIDW
PUI S 0165-5728(00)00292-7
CY Netherlands
DT Journal; General Review
FS 014 Radiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LA English
SL English
AB We studied intrathecal IgG synthesis and autoantibody-secreting cells in 148 patients with possible onset symptoms of MS (POSMS) or clinically definite MS (CDMS). In POSMS intrathecal synthesis of IgG oligoclonal bands and abnormalities on T2-weighted magnetic resonance imaging were associated but the former were more prevalent. The cerebrospinal fluid (CSF) leukocyte count and the number of anti-protelipid protein antibody-secreting cells in cerebrospinal fluid (CSF) correlated with

disease activity in POSMS. Intrathecal IgG synthesis levels and the number of anti-myelin basic protein antibody-secreting cells in CSF correlated with disease activity in CDMS. Our results support recent reports of pathogenetic heterogeneity and a pathogenetic role of the antibody response in MS. Copyright (C) 2000 Elsevier Science B.V.

CT Medical Descriptors:
*immunoglobulin production
*antibody production
***multiple sclerosis: ET, etiology**
cerebrospinal fluid
antibody response
nuclear magnetic resonance imaging
human
male
female
major clinical study
controlled study
adult
review
priority journal
Drug Descriptors:
***immunoglobulin G: EC, endogenous compound**
***autoantibody: EC, endogenous compound**
***myelin basic protein: EC, endogenous compound**
*proteolipid protein: EC, endogenous compound
RN (immunoglobulin G) 97794-27-9

L91 ANSWER 14 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2000107660 EMBASE
TI Autoantibodies in multiple sclerosis.
AU Amor S.; Van Noort H.; Meinl E.
CS Dr. S. Amor, Charing Cross Hospital, London, United Kingdom
SO International MS Journal, (2000) 6/3 (106-107).
Refs: 0
ISSN: 1352-8963 CODEN: IMSJFO
CY United Kingdom
DT Journal; Note
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
LA English
CT Medical Descriptors:
***multiple sclerosis: ET, etiology**
cerebrospinal fluid
immunopathology
isoelectric focusing
human
note
Drug Descriptors:
***autoantibody: EC, endogenous compound**
immunoglobulin G: EC, endogenous compound
myelin associated glycoprotein: EC, endogenous compound
myelin basic protein: EC, endogenous compound
RN (immunoglobulin G) 97794-27-9

L91 ANSWER 15 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:409980 HCAPLUS

DN 133:307005
TI Autoantibodies to acetylcholinesterase revisited
AU Geen, J.; Hadjikoutis, S.; Strachan, A.; Hullin, D. A.; Hogg, S. I.; Wiles, C. M.
CS Clinical Biochemistry Department, Prince Charles Hospital, Mid Glamorgan, Merthyr Tydfil, UK
SO Journal of the Neurological Sciences (2000), 176(1), 37-41
CODEN: JNSCAG; ISSN: 0022-510X
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB A sensitive and specific enzyme linked immunosorbent assay (ELISA) utilizing human recombinant acetylcholinesterase has been employed for the detection of human antibodies to human acetylcholinesterase. The method can detect allogenic antibodies to the Yta form of human erythrocyte AChE. Adaptation of this ELISA method allowed the IgG subclass typing of IgG anti-AChE antibodies, which could help to det. the possible role of these antibodies in the etiol. of any neurol. conditions. Routine serol. investigations established the AChE phenotype of each of the patients recruited, to det. whether anti-AChE antibodies were allogenic or autogenic in origin. These techniques were used to det. the incidence of autoantibodies to AChE in patients with neurol. conditions, including the subtypes of motor neuron disease. The data presented are not consistent with earlier reports of a high incidence of autoantibodies to AChE in amyotrophic lateral sclerosis and progressive muscular atrophy.
CC 7-1 (Enzymes)
Section cross-reference(s): 9, 14, 15
IT Epilepsy
Multiple sclerosis
Parkinson's disease
Spinal muscular atrophy
(application of a new enzyme linked immunosorbent assay for acetylcholinesterase antibodies to several pathologies)
IT **Antibodies**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**autoantibodies; autoantibodies** to acetylcholinesterase)
IT **Immunoassay**
(**enzyme-linked immunosorbent assay;** application of a new **enzyme linked immunosorbent assay** for acetylcholinesterase antibodies to several pathologies)
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 16 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1999285152 EMBASE
TI Demyelination in primate autoimmune encephalomyelitis and acute multiple sclerosis lesions: A case for antigen-specific antibody mediation.
AU Raine C.S.; Cannella B.; Hauser S.L.; Genain C.P.
CS Dr. C.S. Raine, Dept. of Pathology (Neuropathology), Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, United States
SO Annals of Neurology, (1999) 46/2 (144-160).
Refs: 62
ISSN: 0364-5134 CODEN: ANNED3

CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LA English
SL English
AB Neuropathological and ultrastructural features of central nervous system demyelination were compared in marmoset experimental autoimmune encephalomyelitis (EAE) induced with myelin/oligodendrocyte glycoprotein (MEG), and in 3 cases of multiple sclerosis (MS) displaying recent lesions. At the edges of EAE and MS lesions, a zone of myelin vacuolation was common, whereas in the lesion proper, myelin sheaths were consistently transformed into vesiculated membranous networks. These networks became dissociated from axons by cell processes from macrophages. Oligodendrocytes were remarkably spared and evidence of myelin repair was present but not prominent. Axonal pathology was more common in the MS material than in marmoset EAE. Immunocytochemistry, using gold-labeled encephalitogenic peptides of MeG and silver enhancement to detect MeG autoantibodies, revealed the presence of MOG-specific autoantibodies over vesiculated myelin networks. Gold-labeled antibody to IgG also gave a positive reaction. Gold-labeled peptide of myelin basic protein did not react with MOG/EAE tissue, but the same conjugate gave positive staining in MS (and in marmoset EAE induced by whole white matter), perhaps indicating broader spectrum immunoreactivity or sensitization to myelin antigens. Thus, vesicular disruption of myelin was a constant feature in these evolving, highly active lesions in primate EAE and MS and appeared causally related to the deposition of antigen-specific autoantibodies.
CT Medical Descriptors:
*demyelination
*allergic encephalomyelitis
***multiple sclerosis**
antigen specificity
myelin sheath
immunocytochemistry
monkey
neuropathology
human
nonhuman
female
case report
animal experiment
animal model
controlled study
human tissue
animal tissue
adult
article
priority journal
Drug Descriptors:
*myelin
*glycoprotein
***autoantibody: EC, endogenous compound**
*gold
***myelin basic protein**
***immunoglobulin g: EC, endogenous compound**
myelin protein
RN (gold) 7440-57-5; (immunoglobulin g) 97794-27-9

L91 ANSWER 17 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1999237656 EMBASE
TI B-cell responses to myelin basic protein and its epitopes in autoimmune encephalomyelitis induced by Semple rabies vaccine.
AU Piyasirisilp S.; Hemachudha T.; Griffin D.E.
CS D.E. Griffin, Dept. Molecular Microbiol./Immunol., JohnsHopkins University, School of Hygiene and Public Health, 615 N Wolfe Street, Baltimore, MD 21205-2179, United States. dgriffin@welchlink.welch.jhu.edu
SO Journal of Neuroimmunology, (1999) 98/2 (96-104).
Refs: 51
ISSN: 0165-5728 CODEN: JNRIDW
PUI S 0165-5728(99)00065-X
CY Netherlands
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
038 Adverse Reactions Titles
004 Microbiology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LA English
SL English
AB Semple rabies vaccine is composed of rabies virus-infected sheep or goat brain inactivated with phenol and is administered daily after exposure for 14-21 days. Semple rabies vaccine-induced autoimmune encephalomyelitis (SAE) has clinico-pathological findings of demyelination similar to experimental autoimmune encephalomyelitis (EAE) caused by injection of central nervous system tissue or purified myelin proteins into experimental animals and frequently studied as a model for the human demyelinating disease, multiple sclerosis (MS). T-cell-mediated immune responses play a major role in induction of EAE, and antibody responses enhance disease severity. We studied the antibody responses to myelin basic protein (MBP) in 24 Thai patients with SAE and 77 control individuals to define the linear epitopes in human MBP that are encephalitogenic. Antibody levels were assessed by ELISA using native human MBP or synthetic MBP peptides of 20 amino acids. The major B-cell epitope was MBP61-80 and a minor epitope was MBP106-140 in SAE while in MS the major B-cell epitope is MBP84-96. MBP61-80-specific IgG1 and IgG3 levels were significantly higher in patients than controls while IgG2 and IgG4 were not. The data support the hypothesis that autoreactive Th1 cells induce SAE. The difference in B-cell epitope recognition may be due to differences in the genetic backgrounds of the populations studied or may reflect underlying differences in the pathogenesis of SAE and MS.

CT Medical Descriptors:
*antibody response
*allergic encephalomyelitis: SI, side effect
*allergic encephalomyelitis: ET, etiology
*b lymphocyte
***multiple sclerosis: ET, etiology**
amino acid sequence
demyelination
helper cell
enzyme linked immunosorbent assay
human

controlled study
human cell
adult
article
priority journal
Drug Descriptors:
*epitope: EC, endogenous compound
***myelin basic protein**
*rabies vaccine: AE, adverse drug reaction
antibody: EC, endogenous compound
immunoglobulin a
immunoglobulin g
immunoglobulin m
RN (immunoglobulin g) 97794-27-9; (immunoglobulin m) 9007-85-6

L91 ANSWER 18 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1999300479 EMBASE
TI An extensive search for autoantibodies to myelin basic protein in cerebrospinal fluid of non-multiple-sclerosis patients: Implications for the pathogenesis of multiple sclerosis.
AU Warren K.G.; Catz I.
CS Dr. K.G. Warren, MS Patient Care and Research Clinic, Department of Medicine (Neurology), University of Alberta, Edmonton, Alta, T6G 2G3, Canada
SO European Neurology, (1999) 42/2 (95-104).
Refs: 48
ISSN: 0014-3022 CODEN: EUNEAP
CY Switzerland
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
006 Internal Medicine
008 Neurology and Neurosurgery
LA English
SL English
AB Inflammation of multiple sclerosis (MS) brain and spinal cord tissue consists of macrophages, T lymphocytes and cytokines as well as B lymphocytes and immunoglobulins (IgGs). IgG can be detected in high concentrations in both central nervous system tissue and cerebrospinal fluid (CSF). Using a sensitive radioimmunoassay (RIA), autoantibodies to myelin basic protein (anti-MBP) can be detected in the CSF of 90-95% of MS patients with active disease. The purpose of the present report was to determine whether these same autoantibodies can be reliably detected in non-MS patients. Between 1978 and 1998, CSF was collected from 1968 control non-MS patients with psychiatric, inflammatory and noninflammatory neurological diseases as well as nonneurological systemic diseases, and anti-MBP were measured by the same RIA used to detect anti-MBP in MS CSF. Anti-MBP were undetectable in 98% of CSF samples from non-MS controls. In the remaining 2% of control samples, CSF IgGs capable of binding to MBP in vitro were unpredictably detected. This latter group included 1% of patients with miscellaneous diseases such as encephalomyelitis, 5 siblings with familial spastic paraparesis, rare patients with strokes, Wernicke-Korsakoff's syndrome, inherited leukodystrophy, motor neuron disease and some patients with miscellaneous spinal cord diseases. An additional 1% of patients included a group with neurological symptoms suggestive of early or predisseminated MS. The high prevalence of free and/or bound anti-MBP in the CSF of MS patients and the rare and unpredictable occurrence in the CSF of non-MS patients suggest that

autoimmunity to MBP may be operative in the demyelination of MS. Molecular clones of anti-M BP with specificity towards variable surface or cryptic MBP epitopes in vivo may determine whether or not they are involved in the demyelinating process, and this variability may also be present within the MS population. Potential mechanisms of anti-MBP-mediated demyelination in MS patients are discussed.

CT Medical Descriptors:
***multiple sclerosis: ET, etiology**
*cerebrospinal fluid
*antibody detection
pathogenesis
neurologic disease: ET, etiology
systemic disease
mental disease: ET, etiology
inflammatory disease: ET, etiology
encephalomyelitis: ET, etiology
spinal cord disease: ET, etiology
motor neuron disease: ET, etiology
stroke: ET, etiology
Wernicke Korsakoff syndrome: ET, etiology
leukodystrophy: CN, congenital disorder
leukodystrophy: ET, etiology
prevalence
hereditary motor sensory neuropathy: CN, congenital disorder
hereditary motor sensory neuropathy: ET, etiology
demyelination: ET, etiology
human
male
female
major clinical study
aged
adult
article
priority journal
Drug Descriptors:
***autoantibody: EC, endogenous compound**
***myelin basic protein: EC, endogenous compound**
immunoglobulin g: EC, endogenous compound
RN (immunoglobulin g) 97794-27-9

L91 ANSWER 19 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:728653 HCAPLUS
DN 130:3055
TI Early detection of autoimmune inflammation by detection of autoantibodies to specific markers
IN Petry, Klaus; Boullerne, Anne
PA Institut National de la Sante et de la Recherche Medicale (INSERM), Fr.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9849558	A1	19981105	WO 1998-FR853	19980428

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE
FR 2762602 A1 19981030 FR 1997-5228 19970428
FR 2762602 B1 19990604
EP 980525 A1 20000223 EP 1998-922887 19980428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002506516 T2 20020226 JP 1998-546675 19980428
PRAI FR 1997-5228 A 19970428
WO 1998-FR853 W 19980428

AB A method of early diagnosis of inflammatory autoimmune disease by detection of autoantibodies to fatty acids and to protein amino acid nitrites, specifically protein cysteine nitrite is described. Rats with exptl. autoimmune encephalomyelitis were assayed for antibodies to cysteine nitrite and to fatty acids using conjugates with bovine serum albumin. These rats had circulating IgM against cysteine nitrite, but not IgG in the early stages of the disease (at about 6 days), but they disappeared as the disease progressed. This was accompanied by a loss of strength (50-60%) in the hind leg muscles between days 18 and 26 post-induction. A correlation was found between antibody titers and demyelination in the brain. Myelin-assocd. glycoprotein and myelin-oligodendroglial glycoprotein were identified as targets for these antibodies.

IC ICM G01N033-564
ICS G01N033-92; G01N033-68
CC 15-1 (Immunochemistry)
IT **Antibodies**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**autoantibodies**, as diagnostic markers; early detection of autoimmune inflammation by detection of **autoantibodies** to specific markers)
IT **Multiple sclerosis**
(early diagnosis of; early detection of autoimmune inflammation by detection of autoantibodies to specific markers)
IT **Immunoassay**
(**enzyme-linked immunosorbent assay**, for autoantibodies; early detection of autoimmune inflammation by detection of autoantibodies to specific markers)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 20 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:268515 HCAPLUS
DN 128:320549
TI Materials and method for the detection and treatment of Wegener's granulomatosis
IN Staud, Roland
PA University of Florida, USA
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9817681	A1	19980430	WO 1997-US19145	19971017

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS,

JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SD, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	AU 9749154	A1	19980515	AU 1997-49154	19971017
	US 6033915	A	20000307	US 1997-953327	19971017
	US 6277955	B1	20010821	US 1999-472579	19991227
PRAI	US 1996-28701P	P	19961018		
	US 1997-953327	A1	19971017		
	WO 1997-US19145	W	19971017		

AB The subject invention pertains to the identification of peptides useful in the detection and treatment of Wegener's granulomatosis. The peptides are fragments or variants of autoimmune disease-assocd. antigen and proteinase-3. These peptides are also useful for ELISA or RIA diagnosis and immunotherapy of other autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, insulin dependent diabetes, myasthenia gravis, Grave's disease and vitiligo.

IC ICM C07K007-06
ICS C07K016-40; C12N009-64

CC 15-2 (Immunochemistry)
Section cross-reference(s): 9

IT **Antibodies**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**autoantibodies**; proteinase-3 fragments or variants for diagnosis and immunotherapy of Wegener's granulomatosis and autoimmune diseases)

IT **Immunoassay**
(**enzyme-linked immunosorbent assay**; proteinase-3 fragments or variants for diagnosis and immunotherapy of Wegener's granulomatosis and autoimmune diseases)

IT Autoimmune disease
Graves' disease
Immunotherapy
Multiple sclerosis
Myasthenia gravis
Protein sequences
Rheumatoid arthritis
Vitiligo
(proteinase-3 fragments or variants for diagnosis and immunotherapy of Wegener's granulomatosis and autoimmune diseases)

L91 ANSWER 21 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1998301544 EMBASE
TI MBP, anti-MBP and anti-PLP antibodies, and intrathecal complement activation in multiple sclerosis.
AU Sellebjerg F.; Christiansen M.; Garred P.
CS F. Sellebjerg, The MS Clinic, Department of Neurology, Glostrup Hospital, Copenhagen, Denmark
SO Multiple Sclerosis, (1998) 4/3 (127-131).
Refs: 46
ISSN: 1352-4585 CODEN: MUSCFZ
CY United Kingdom
DT Journal; Article
FS 008 Neurology and Neurosurgery

026 Immunology, Serology and Transplantation
LA English
SL English
AB Intrathecal immunoglobulin synthesis and activation of the complement cascade occurs in patients with multiple sclerosis (MS). The Present study aimed at further studying the relation between intrathecal immunoglobulin synthesis and complement activation. We compared total intrathecal synthesis of IgA, IgG, and IgM, the number of cells secreting anti-myelin basic protein (MBP) and anti-proteolipid protein (PLP) antibodies of the IgG isotype and intrathecal activation of the complement cascade in patients with possible onset symptoms of MS (n = 18) or clinically definite MS (n = 30). Early activation of the complement cascade correlated with intrathecal synthesis of IgM. Intrathecal IgG, IgA and IgM synthesis also correlated weakly with the presence of cells secreting anti-MBP or anti-PLP autoantibodies. Full activation of the complement cascade did not correlate with any measures of intrathecal antibody synthesis. These findings suggest a complex relation between different immunoglobulin isotypes and complement activation which may have similarly complex roles in the pathogenesis of MS.
CT Medical Descriptors:
***multiple sclerosis: ET, etiology**
*complement activation
*cerebrospinal fluid
immunoglobulin production
human
clinical article
animal cell
article
Drug Descriptors:
***myelin basic protein: EC, endogenous compound**
*proteolipid protein: EC, endogenous compound
***autoantibody: EC, endogenous compound**
immunoglobulin g antibody: EC, endogenous compound
immunoglobulin m: EC, endogenous compound
immunoglobulin a: EC, endogenous compound
RN (immunoglobulin m) 9007-85-6

L91 ANSWER 22 OF 39 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 1998-44421 DRUGU A G
TI Combining **ELISA**, RP-HPLC, and SDS-PAGE to define the potency of a complex biologic.
AU Zabrecky J R; Brown E K; Compton B J; Kretschmer M W; Fowler E; Bernardy J D
CS Autoimmune-Inc.; Waters; Biogen
LO Lexington, Milford; Cambridge, Mass., USA
SO Pharm.Technol. (22, No. 10, 36-45, 1998) 7 Fig. 7 Ref.
CODEN: PTECDN ISSN: 0147-8087
AV Autoimmune Inc., 128 Spring St., Lexington, MA 01239, U.S.A. (J.D.B.). (e-mail: zabrecky@erols.com).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Myloral was developed as a p.o. tolerance therapy for **multiple sclerosis**, and is thought to operate via amplifying a population of antigen-specific helper T cells. It is derived from bovine CNS, and is a complex mixture of about 30% proteins, 60% lipids, and 10% sucrose.

The 2 principal proteins, **myelin basic protein** (**MBP**) and proteolipid protein (PLP) act as p.o. tolerogens. **ELISA**, RP-HPLC, and SDS-PAGE methodologies were developed in order to define the potency of Myloral. HPLC and SDS-PAGE were validated in stability studies on Myloral. **ELISA** was used to monitor the stability of total Myloral antigen (TMA). The combined strategy quantified dose, ensured both content uniformity and consistency of immunological epitopes.

L91 ANSWER 23 OF 39 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 1997-11864 DRUGU T S
TI **Heparin**-induced thrombocytopenia and thrombosis: a prospective analysis of the incidence in patients with heart and cerebrovascular diseases.
AU Kappers Klunne M C; Boon D M S; Hop W C J; Michiels J J; Stibbe J; Zwaan C Van Der; Koudstaal P J; Vliet H H D M Van
CS Univ.Rotterdam
LO Rotterdam, Neth.
SO Br.J.Haematol. (96, No. 3, 442-46, 1997) 2 Fig. 2 Tab. 13 Ref.
CODEN: BJHEAL ISSN: 0007-1048
AV Department of Haematology, University Hospital Rotterdam, The Netherlands.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The incidence of serologically-confirmed **heparin**-induced thrombocytopenia and/or thrombosis (HITT) was very low in a prospective study of 358 patients with heart and cerebrovascular diseases given therapeutic-dose i.v. unfractionated **heparin** (UFH). However, the frequency of **heparin**-dependent Abs was much higher. **Heparin** was withdrawn and danaparoid treatment started in a patient with end-stage renal failure who developed a thrombosis at a catheter insertion site. Half the patients received concomitant aspirin. HITT is rare in patients given unfractionated **heparin** for heart and cerebrovascular disease, but the frequency of **heparin** -dependent Abs is higher.

L91 ANSWER 24 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 97203688 EMBASE
DN 1997203688
TI High levels of cerebrospinal fluid IgM binding to myelin basic protein are associated with early benign course in multiple sclerosis.
AU Annunziata P.; Pluchino S.; Martino T.; Guazzi G.
CS P. Annunziata, Institute of Neurological Sciences, University of Siena, Viale Bracci 2, 53100 Siena, Italy. annunziata@unisi.it
SO Journal of Neuroimmunology, (1997) 77/1 (128-133).
Refs: 26
ISSN: 0165-5728 CODEN: JNRIDW
PUI S 0165-5728(97)00074-X
CY Netherlands
DT Journal; Article
FS 008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
LA English
SL English
AB We assessed human myelin basic protein (MBP) binding IgM levels in the

CSF. MBP is the most studied putative antigen in multiple sclerosis (MS) and immune responses directed against it may be involved in the demyelination process. We also correlated these levels with EDSS score and other parameters of disease progression and prognosis, both at the time of CSF analysis and during follow-up. CSF IgM anti-MBP levels were assayed by measuring total lgM levels with solid-phase ELISA in CSF samples from 66 patients with relapsing remitting MS, II subjects without neurological diseases. 20 patients with non-inflammatory neurological diseases and 7 patients with lymphocytic meningitis, before and after immunoabsorption with human MBP. Confirmation of lgM binding specificity was performed by immunoblotting of positive CSF samples onto MBP coated-nitrocellulose sheets. Clinical evaluation (disability score, number and time of attacks) was performed during a mean follow-up of 2.7 .+-. 1.1 years, 23 of 66 relapsing-remitting MS patients (33.8%) had elevated IgM anti-MBP levels. In this patient subgroup, IgM anti- MBP levels correlated with the IgM index (r = 0.71; P = 0.0001), but not with CSF/serum albumin (r = 0.08; P = 0.72). In the first year of follow up, patients with low IgM anti-MBP suffered from more numerous attacks than those with elevated levels (0.86 .+-. 0.63 versus 0.43 .+-. 0.58; P = 0.017). Patients with high IgM binding to MBP had a first attack during follow up in a significantly higher time than those with low binding (28.87 .+-. 4.7 versus 17 .+-. 2.6 months, respectively; P = 0.005) and reached a decrease of 0.5 EDSS point significantly faster than those with low IgM (16.17 .+-. 1.2 versus 29.7 .+-. 2.6 months, respectively; P = 0.0002). A similar significant finding was observed when the time to reach low disability score (EDSS .ltoreq. 2.0) was analyzed (10.7 .+-. 2 versus 25.7 .+-. 3.3 months, respectively: P = 0.014). These findings demonstrate that in a subgroup of MS patients, elevated CSF levels of IgM anti-MBP are associated with early favorable course and therefore suggest that IgM binding to MBP could be a possible prognostic marker in relapsing-remitting MS to select early MS patients for future trials.

CT Medical Descriptors:
*cerebrospinal fluid
***multiple sclerosis**
adult
article
autoimmunity
b lymphocyte
cerebrospinal fluid analysis
controlled study
demyelination: ET, etiology
disability
disease course
enzyme linked immunosorbent assay
female
human
immune response
immunoadsorption
immunoblotting
major clinical study
male
meningitis
neurologic disease
priority journal
prognosis
protein binding
Drug Descriptors:

***immunoglobulin m**
***myelin basic protein**
RN (immunoglobulin m) 9007-85-6

L91 ANSWER 25 OF 39 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 1997-43575 DRUGU P A G
TI An HPLC/**MS**/**MS** assay for tacrolimus in patient blood samples. Correlation with results of an **ELISA** assay.
AU Alak A M; Moy S; Cook M; Lizak P; Niggebiugge A; Menard S; Chilton A
CS Fujisawa; Phoenix
LO Evanston, Ill., USA; Montreal, Que., Can.
SO J.Pharm.Biomed.Anal. (16, No. 1, 7-13, 1997) 2 Fig. 2 Tab. 16 Ref.
CODEN: JPBADA ISSN: 0731-7085
AV Fujisawa Research Institute of America, Northwestern University/Evanston Research Park, 1801 Maple Ave, Evanston, IL 60201, USA.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB An HPLC/**MS**/**MS** method has been developed for the determination of tacrolimus (Fujisawa) in patient blood samples. The new method had increased sensitivity (limit of sensitivity 0.1 ng/ml) compared to currently available immunoassay methods: IMx (5 ng/ml) and **ELISA** (0.5 ng/ml). The new method correlated well with the immunoassay methods when compared in a pharmacokinetic study of atopic dermatitis patients receiving topical tacrolimus ointment, and when used to screen blood samples from organ transplant patients receiving tacrolimus.

L91 ANSWER 26 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:334788 HCAPLUS
DN 126:308824
TI Low-molecular-weight heparins for inhibition of tumor necrosis factor-.alpha. secretion
IN Cohen, Irun R.; Lider, Ofer; Hershkovitz, Rami
PA Yeda Research and Development Co Ltd, Israel
SO Israeli, 41 pp.
CODEN: ISXXAQ
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	IL 98028	A1	19961205	IL 1991-98028	19910502
	EP 583360	A1	19940223	EP 1992-911373	19920501
	EP 583360	B1	20020522		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	BR 9205961	A	19940726	BR 1992-5961	19920501
	AT 217796	E	20020615	AT 1992-911373	19920501
	NO 9303942	A	19931214	NO 1993-3942	19931101
	US 5474987	A	19951212	US 1995-384203	19950203
	US 5686431	A	19971111	US 1995-457655	19950601
	US 5908837	A	19990601	US 1997-966315	19971107
PRAI	IL 1991-98028	A	19910502		
	IL 1991-98298	A	19910528		
	US 1992-878188	B1	19920501		
	WO 1992-US3626	W	19920501		

US 1995-384203 A1 19950203
US 1995-457655 A1 19950601

AB The present invention relates to pharmaceutical compns. for the prevention and/or treatment of pathol. processes involving the induction of TNF-.alpha. secretion comprising a pharmaceutically acceptable carrier and a low mol. wt. heparin (LMWH). In the pharmaceutical compns. of the present invention, the LMWH is present in a low ED and is administered at intervals of about 5-8 days. Furthermore, the LMWH is capable of inhibiting in vitro TNF-.alpha. secretion by resting T cells and/or macrophages in response to T cell-specific antigens, mitogens, macrophage activators, disrupted extracellular matrix (dECM), laminin, fibronectin, and the like.

IC ICM A61K031-725

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT AIDS (disease)
Allergy inhibitors
Anti-inflammatory agents
Antirheumatic agents
Autoimmune disease
Immunosuppressants
Macrophage
Mitogens
Multiple sclerosis
(low-mol.-wt. heparins for inhibition of tumor necrosis factor-.alpha. secretion)

IT Fibronectins
Laminins
Myelin basic protein
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(low-mol.-wt. heparins for inhibition of tumor necrosis factor-.alpha. secretion)

IT **9005-49-6**, Heparin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-mol.-wt. heparins for inhibition of tumor necrosis factor-.alpha. secretion)

L91 ANSWER 27 OF 39 DRUGU COPYRIGHT 2002 THOMSON DERWENT

AN 1997-02546 DRUGU T M S

TI Prevalence of anti-thyroid **autoantibodies** before and after interferon treatment in patients with HCV infection and beta-thalassemia major in Greece.

AU Mimidis K; Goritsas K; Matsouka P; Margaritis V

LO Patras, Gr.

SO Gut (39, Suppl. 3, A113, 1996)
CODEN: GUTTAK ISSN: 0017-5749

AV Department of Internal Medicine, University Hospital of Patras, Patras, Greece.

LA English

DT Journal

FA AB; LA; CT

FS Literature

AB The prevalence of antithyroid **autoantibodies** varies in reports from different countries. A high prevalence of antithyroid antibodies in

chronic hepatitis C especially after interferon (IFN) treatment is already reported. The Authors studied the prevalence of antimicrosomal antibodies in Greece in 24 multitransfused thalassemic patients and in otherwise healthy patients with chronic hepatitis C. Epidemiologic data in general population of the Authors region (SW Greece) report a prevalence for antithyroid antibodies of 12%. Results suggest that 1) prevalence of **autoantibody** in Greek patients with HCV infection does not differ from that observed in general population; 2) patients with beta-thalassemia major had a zero prevalence of antithyroid antibodies; 3) IFN did not influence the thyroid function in antithyroid **autoantibody** negative patients. (conference abstract).

L91 ANSWER 28 OF 39 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 1997-03367 DRUGU P A
TI An HPLC/**MS**/**MS** assay for tacrolimus in patient samples. Correlation with results of an **elisa** assay.
AU Alak A M; Cook M; Moy S; Lessand D
CS Fujisawa; Phoenix-Int.Life-Sciences
LO Chicago, Ill., USA; Montreal, Que., Can.
SO Pharm.Res. (13, No. 9, Suppl., S39, 1996)
CODEN: PHREEB ISSN: 0724-8741
AV Fujisawa USA, Inc., Chicago, IL 60612, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB An HPLC/**MS**/**MS** assay for tacrolimus in whole blood using FR-900520 as an internal standard was validated over the standard curve range of 0.100 to 10.040 ng/ml. The correlation between assay results by HPLC/**MS**/**MS** and ELlSA in whole blood from patients undergone solid organ transplantation that received oral dosage of tacrolimus was determined. Also, blood from atopic dermatitis patients received treatment with tacrolimus ointment showed a good correlation between the two assay methods. (conference abstract).

L91 ANSWER 29 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 95148728 EMBASE
DN 1995148728
TI Intrathecal immune response in patients with neuroborreliosis: Specificity of antibodies for neuronal proteins.
AU Kaiser R.
CS Neuroimmunological Laboratory, Department of Neurology, University of Freiburg, Breisacher Strasse 64,D-79106 Freiburg, Germany
SO Journal of Neurology, (1995) 242/5 (319-325).
ISSN: 0340-5354 CODEN: JNRYA
CY Germany
DT Journal; Article
FS 004 Microbiology
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
LA English
SL English
AB Cerebrospinal fluid (CSF) and serum samples of 47 patients with serologically proven neuroborreliosis were examined by Western blotting for antibodies to a crude extract of human cortex (CNS) comprising a multitude (> 40) of protein bands. Intrathecal synthesis of total immunoglobulins was determined by the Reiber formula and of autoantibodies

to CNS proteins by enzyme-linked immunoassay (ELISA) and by Western blotting. Employing ELISA, intrathecal synthesis of autoantibodies (IgG, IgM and/or IgA) was demonstrated in 40 of 47 patients with neuroborreliosis (85%), in 5 of 40 with multiple sclerosis (12%), and in 22 of 40 with viral meningoencephalitis (55%). Of 40, 35 and 15 patients with neuroborreliosis and an intrathecal synthesis of total IgG, IgM or IgA, 20 revealed an intrathecal production of IgG antibodies (50%), 24 of IgM antibodies (68%) and 6 of IgA autoantibodies (40%) in the CSF. The specificity of autoantibodies differed greatly between most patients. Of 24 different CNS proteins which elicited an immune response in various patients, identities could be determined only for the myelin basic protein (5 of 40) and for the three neurofilament proteins (NF-68, NF-150, NF-200) (13 of 40 patients). In this limited number of patients no significant correlation between individual clinical symptoms and certain autoantibodies could be detected. The higher frequency of intrathecally produced autoantibodies in patients with neuroborreliosis is assumed to result from mitogenic rather than specific activation of autoreactive B-cell clones by Borrelia burgdorferi. The pathogenic relevance of these autoantibodies remains to be determined.

CT Medical Descriptors:
*autoimmunity
*borrelia infection: ET, etiology
antibody specificity
article
blood analysis
borrelia burgdorferi
cerebrospinal fluid
cerebrospinal fluid analysis
clinical article
controlled study
enzyme linked immunosorbent assay
female
human
immunoblotting
immunoglobulin production
immunopathogenesis
male
meningoencephalitis
multiple sclerosis
priority journal
etiology
Drug Descriptors:
***autoantibody: EC, endogenous compound**
*immunoglobulin a: EC, endogenous compound
***immunoglobulin g: EC, endogenous compound**
***immunoglobulin m: EC, endogenous compound**
myelin basic protein: EC, endogenous compound
neurofilament protein: EC, endogenous compound

RN (immunoglobulin g) 97794-27-9; (immunoglobulin m) 9007-85-6

L91 ANSWER 30 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:699105 HCAPLUS
DN 121:299105
TI Method and kit for detecting and/or quantifying different classes of immunoglobulins specific for an autoimmune disease.
IN Maes, Roland; Causse, Jean-Etienne; Labrousse, Hossein
PA Anda Biologicals S.A., Fr.

SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 621479	A1	19941026	EP 1994-870069	19940419
	R: DE, FR, GB, IT				
	BE 1006974	A3	19950207	BE 1993-413	19930423
PRAI	BE 1993-413		19930423		

AB The title method involves reacting the Igs of sample body fluid with an antigenic conjugate specific for the pathol., e.g., a fatty acid or a phospholipid conjugated with a water-sol. protein, and with a labeled reagent specific for an Ig class. The Ig classes of autoantibodies to oleic acid were detd. in blood serum samples from patients with multiple sclerosis by ELISA using immobilized oleic acid conjugated with thyroglobulin and peroxidase-labeled antibodies to human IgG, IgA, and IgM.
IC ICM G01N033-564
ICS G01N033-92
CC 15-1 (Immunochemistry)
IT Autoimmune disease
Blood analysis
Body fluid
Immunoassay
Multiple sclerosis
(method and kit for detecting and/or detg. different classes of Igs specific for autoimmune disease)
IT **Antibodies**
RL: ANT (Analyte); ANST (Analytical study)
(**auto-**, method and kit for detecting and/or detg. different classes of Igs specific for autoimmune disease)
IT **Immunoassay**
(**enzyme-linked immunosorbent assay**, method and kit for detecting and/or detg. different classes of Igs specific for autoimmune disease)

L91 ANSWER 31 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:455398 HCAPLUS
DN 121:55398
TI ELISA-type titertray assay for IgM anti-GM1 autoantibodies
AU Bech, Einar; Jakobsen, Johannes; Oerntoft, Torben F.
CS Dep. Clin. Chem., Aarhus Univ. Hosp., Aarhus, DK 8000, Den.
SO Clinical Chemistry (Washington, DC, United States) (1994), 40(7, Pt. 1), 1331-4
CODEN: CLCHAU; ISSN: 0009-9147
DT Journal
LA English
AB The authors report an ELISA-type titertray assay for autoantibodies against the ganglioside GM1. Trays were coated with ganglioside GM1 and reacted with patients' sera; bound IgM was detected with rabbit antibody to human IgM. Higher-titer serum from a patient was used as calibrator, another patient's serum as the pos. control, and the GM1-specific cholera toxin as the control for GM1 coating. Regression curves of serum titers obtained from different patients were linear and parallel. Intra- and inter-assay CVs were 4.0-7.8% and 5.5-16%, resp. The authors detected

antibodies at a titer of 1:250 in normal subjects. Anal. specificity of the calibrator serum against GM1 was demonstrated by immune thin-layer chromatog. Anti-GM1 antibodies were increased in patients with chronic inflammatory demyelinating polyradiculoneuropathy or multiple sclerosis. In Guillain-Barre syndrome, preliminary longitudinal studies showed a decrease in anti-GM1 titer that was related to clin. recovery.

CC 15-1 (Immunochemistry)

IT **Multiple sclerosis**
(IgM autoantibody to ganglioside GM1 in humans with, detection of, by titertray ELISA)

IT **Immunoglobulins**
RL: BIOL (Biological study)
(**auto-, M,** to ganglioside GM1, detection of human, by titertray ELISA)

IT **Immunoassay**
(**enzyme-linked immunosorbent assay,** titertray, IgM autoantibodies to ganglioside GM1 detection by, in humans)

L91 ANSWER 32 OF 39 MEDLINE
AN 95141775 MEDLINE
DN 95141775 PubMed ID: 7530889
TI Intrathecal synthesis of anti-myelin basic protein IgG in HIV-1+ patients.
AU Maimone D; Annunziata P; Cioni C; Leonardi A; Guazzi G C
CS Institute of Neurological Sciences, University of Siena, Italy.
SO ACTA NEUROLOGICA SCANDINAVICA, (1994 Oct) 90 (4) 285-92.
Journal code: 0370336. ISSN: 0001-6314.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199502
ED Entered STN: 19950314
Last Updated on STN: 19970203
Entered Medline: 19950228
AB Human immunodeficiency virus type 1 (HIV-1)-infected individuals frequently develop a broad spectrum of neurological syndromes, classified as HIV-1-associated cognitive/motor complex. Diffuse demyelination of hemispheric white matter is a commonly observed in HIV-1 infected brain, but the events leading to myelin destruction are still obscure. Since oligodendrocyte infection by HIV-1 is not proven as yet, myelin damage in HIV-1 infection may result from indirect mechanisms such as the excessive release of myelinotoxic substances or the triggering of autoimmune responses directed to myelin constituents. To verify the latter hypothesis, we searched for elevated anti-myelin basic protein (MBP) IgG levels in the cerebrospinal fluid (CSF) and serum of 25 patients with HIV-1 infection, 12 with multiple sclerosis (MS), and 9 with non-inflammatory neurological diseases (NIND). CSF, but not serum, anti-MBP IgG levels were more frequently elevated in HIV-1+ (16/25, 64%) than in MS (3/12, 25%) or NIND (0/9) patients. By using the anti-MBP IgG index, the anti-MBP IgG antibody specificity index (ASI), and the search for anti-MBP oligoclonal IgG, we ascertained that anti-MBP IgG were produced within the CNS in 13 of 25 (52%) HIV-1+, in 6 of 12 (50%) MS, and in none of NIND patients. The incidence of increased CSF anti-MBP IgG levels was higher among HIV-1+ patients at stage II-III (4/4, 100%) or at stage IV B (7/9, 78%) than among those at stage IV C-IV D (5/12, 42%). Although our data indicate that intrathecal anti-MBP IgG may occur early

during HIV-1 infection and that they are more common in patients with HIV-1-associated cognitive/motor complex, the possible demyelinating role of these antibodies remains to be demonstrated.

CT Check Tags: Human; Support, Non-U.S. Gov't
AIDS Dementia Complex: DI, diagnosis
*AIDS Dementia Complex: IM, immunology
***Autoantibodies: CF, cerebrospinal fluid**
Blood-Brain Barrier: IM, immunology
Diagnosis, Differential
Enzyme-Linked Immunosorbent Assay
HIV Seropositivity: DI, diagnosis
*HIV Seropositivity: IM, immunology
*HIV-1: IM, immunology
***Immunoglobulin G: CF, cerebrospinal fluid**
Immunoglobulins: CF, cerebrospinal fluid
Multiple Sclerosis: DI, diagnosis
Multiple Sclerosis: IM, immunology
***Myelin Basic Proteins: IM, immunology**
Myelin Sheath: IM, immunology
Nervous System Diseases: DI, diagnosis
Nervous System Diseases: IM, immunology
Neurologic Examination
Neuropsychological Tests

CN 0 (Autoantibodies); 0 (Immunoglobulin G); 0 (Immunoglobulins); 0 (Myelin Basic Proteins); 0 (oligoclonal immunoglobulins)

L91 ANSWER 33 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 94099781 EMBASE
DN 1994099781
TI Anti-myelin basic protein and anti-proteolipid protein specific forms of multiple sclerosis.
AU Warren K.G.; Catz I.; Johnson E.; Mielke B.
CS Department of Medicine (Neurology), MS Patient Care and Research Clinic, University of Alberta,Edmonton, Alta. T6G 2G3, Canada
SO Annals of Neurology, (1994) 35/3 (280-289).
ISSN: 0364-5134 CODEN: ANNED3
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
LA English
SL English
AB Human myelin basic protein (hMBP) and proteolipid protein (PLP) were used as antigens in a solid-phase radioimmunoassay to determine relative frequencies of anti-MBP and anti-PLP in cerebrospinal fluid (CSF) of optic neuritis and multiple sclerosis (MS) patients. Forty-nine of 55 patients with optic neuritis had increased CSF anti-MBP and the remaining 6 had increased anti-PLP. Of 385 MS patients, MS relapse: 173 of 180 patients had increased anti-MBP, 5 of the remaining 7 patients had elevated anti-PLP, and 2 had neither of these autoantibodies. Progressive MS: 111 of 116 patients had increased anti-MBP in either free and/or bound form, of the remaining 5 patients 4 had increased anti-PLP, and 1 had neither anti-MBP nor anti-PLP. MS remission: 15 of 87 patients had somewhat increased anti-MBP, none had anti-PLP. IgG was purified by affinity chromatography from necropsy central nervous system (CNS) tissue samples of 4 individual patients with clinically definite and neuropathologically

confirmed MS. Three of these 4 patients who had increased levels of CSF anti-MBP also had increased anti-MBP titers in CNS tissue-extracted IgG. The fourth patient who had anti-PLP in CSF also had anti-PLP in brain tissue IgG. These autoantibodies were not detected simultaneously in any patient. These results suggest that there are at least two immunologically distinct forms of MS, i.e., a common form highly associated with anti-MBP and more frequent prominent inflammatory characteristics in CSF and CNS, and an infrequent form associated with anti- PLP in CSF and tissue, and less abundant inflammation. Anti-MBP purified from CNS tissue IgG by antigen-specific affinity chromatography was reacted with synthetic peptides of hMBP. The anti-MBP epitope on the hMBP molecule was restricted between residues 75 and 106. The PLP epitope for anti-PLP has not as yet been determined. These observations have theoretical implications for anticipated future specific immunotherapy of MS.

CT Medical Descriptors:
*cerebrospinal fluid analysis
***multiple sclerosis**
*optic neuropathy
affinity chromatography
article
human
human tissue
major clinical study
priority journal
radioimmunoassay
relapse
remission
Drug Descriptors:
***autoantibody: EC, endogenous compound**
*epitope: EC, endogenous compound
***immunoglobulin g: EC, endogenous compound**
***myelin basic protein**
*proteolipid protein
*synthetic peptide
RN (immunoglobulin g) 97794-27-9

L91 ANSWER 34 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:16313 HCAPLUS
DN 118:16313
TI Prevention and/or treatment of pathological processes related to tumor necrosis factor .alpha.
IN Cohen, Irun R.; Lider, Ofer; Hershkoviz, Rami
PA Yeda Research and Development Co. Ltd., Israel
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9219249	A1	19921112	WO 1992-US3626	19920501
	W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	AU 9219131	A1	19921221	AU 1992-19131	19920501
	AU 668865	B2	19960523		

	EP 583360	A1	19940223	EP 1992-911373	19920501
	EP 583360	B1	20020522		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	BR 9205961	A	19940726	BR 1992-5961	19920501
	JP 06507635	T2	19940901	JP 1992-511483	19920501
	HU 67136	A2	19950228	HU 1993-3110	19920501
	AT 217796	E	20020615	AT 1992-911373	19920501
	NO 9303942	A	19931214	NO 1993-3942	19931101
PRAI	IL 1991-98020	A	19910502		
	IL 1991-98298	A	19910528		
	IL 1991-98028	A	19910502		
	WO 1992-US3626	A	19920501		

AB Low mol. wt. heparin (LMWH), administered s.c. or i.v., at 5-8 day intervals, inhibits in vitro secretion of tumor necrosis factor-.alpha. by resting T-cells or macrophages, in response to T-cell-specific antigens, nitrogens, macrophage activators, disrupted extracellular matrix, laminin, fibronectin, or other extracellular matrix components. LMWH is useful for the prevention and treatment of allograph rejection, autoimmune disease, allergy, inflammatory diseases, AIDS, etc. rats administered s.c. 20 .mu.g Fragmin (LMWH), at 7 day intervals, showed increased survival of heart allographs.

IC ICM A61K031-725

CC 1-7 (Pharmacology)

IT Acquired immune deficiency syndrome
Arthritis
Multiple sclerosis
(treatment of, with low-mol.-wt. heparin)

IT **Phospholipoproteins**
RL: BIOL (Biological study)
(**MBP** (**myelin basic protein**),
pharmaceutical compn. contg. low mol. wt. heparin and, for inhibiting delayed type hypersensitivity)

IT **9005-49-6**, Clexane, biological studies 9041-08-1
RL: BIOL (Biological study)
(for treatment of diseases and disorders involving tumor necrosis factor-.alpha.)

L91 ANSWER 35 OF 39 HCAPLUS COPYRIGHT 2002 ACS

AN 1992:649884 HCAPLUS

DN 117:249884

TI Means and methods for in vitro diagnosis of multiple sclerosis and other demyelinating neuropathies using inositol group antigens

IN Geffard, Michel

PA Institut des Neurosciences Cliniques, Fr.

SO Fr. Demande, 29 pp.
CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2667945	A1	19920417	FR 1990-12578	19901011

AB Multiple sclerosis and other demyelinating diseases are diagnosed by using the inositol group as antigenic determinant. Kits for the assay comprise inositol-contg. antigens and solvents, buffers, and agents necessary for carrying out the assay. An ELISA was used to detect anti-phosphatidylinositol autoantibodies in the blood serum of multiple

sclerosis patients.
IC ICM G01N033-92
ICS G01N033-564
CC 15-1 (Immunochemistry)
Section cross-reference(s): 9
IT **Multiple sclerosis**
(immunodiagnosis of, anti-inositol antibodies detn. in)
IT **Antibodies**
RL: PROC (Process)
(**auto-**, to phosphatidylinositol, detn. of, in blood by ELISA, for multiple sclerosis diagnosis)
IT **Immunoassay**
(**enzyme-linked immunosorbent assay**, anti-phosphatidylinositol autoantibodies detn. by, in diagnosis of multiple sclerosis)

L91 ANSWER 36 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 91176446 EMBASE
DN 1991176446
TI Cord blood contains cells secreting antibodies to nervous system components.
AU Fredrikson S.; Sun J.; Xiao B.-G.; Link H.
CS Department of Neurology, Karolinska Institutet, Huddinge University Hospital,S-141 86 Huddinge, Sweden
SO Clinical and Experimental Immunology, (1991) 84/2 (353-358).
ISSN: 0009-9104 CODEN: CEXIAL
CY United Kingdom
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
LA English
SL English
AB Umbilical cord blood of newborns and peripheral blood of healthy adults were investigated by an immunospot assay for cells secreting IgG, IgA and IgM antibodies against myelin basic protein (MBP), proteolipid protein (PLP), myelin-associated glycoprotein (MAG) and myelin oligodendrocyte glycoprotein (MOG) which represent putative antigens for an autoimmune attack in multiple sclerosis (MS) and against acetylcholine receptor (AChR) which is considered an important autoantigen in myasthenia gravis. Cells secreting antibodies against one or more of these autoantigens were detected in 18 out of 24 newborns, and in eight out of 20 adults. Eight of the cord blood samples contained cells secreting antibodies of IgG, IgA and/or IgM isotypes to one antigen, five to two antigens, two to three antigens, two to four antigens, and one to five antigens. Most prominent were anti-MBP IgG antibody secreting cells which were detected in 13 newborns at a mean number of 1/20,000 cord blood cells, and in six adults at a mean number of 1/105 peripheral blood cells. Anti-AChR IgG antibody secreting cells were detected in four out of 12 newborns versus four out of 14 peripheral blood specimens, at mean values of 1/105 cells in both instances. Cells secreting autoantibodies of IgA and IgM isotypes were less frequent both in cord blood and peripheral blood. The occurrence of nervous tissue autoantibody secreting cells in newborns must be related to a possible primary role of such autoantibodies in MS and myasthenia gravis.
CT Medical Descriptors:
***multiple sclerosis: ET, etiology**

*myasthenia gravis: ET, etiology
*umbilical cord blood
adult
article
enzyme linked immunosorbent assay
female
human
male
newborn
normal human
priority journal
Drug Descriptors:
***autoantibody: EC, endogenous compound**
*cholinergic receptor antibody: EC, endogenous compound
***myelin basic protein: EC, endogenous compound**

L91 ANSWER 37 OF 39 HCAPLUS COPYRIGHT 2002 ACS
AN 1990:474282 HCAPLUS
DN 113:74282
TI Immunoassay of myelin P2 protein in body fluids for detection of demyelination and diagnosis of multiple sclerosis
IN Colover, Jack
PA UK
SO Brit. UK Pat. Appl., 11 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2224837	A1	19900516	GB 1988-25832	19881104
GB 2224837	B2	19921007		

AB A method of detecting and/or monitoring a demyelination process liable to occur in multiple sclerosis (MS) and viral diseases of the nervous system comprises an immunoassay for myelin P2 protein and/or fragments in a body fluid using a polyclonal or monoclonal antibody raised against P2 protein. The method is particularly useful for the diagnosis and monitoring of MS. The method is carried out by ELISA on samples of spinal fluid from patients suffering from MS. Assay is made by incubating rabbit anti-P2 antibody with a serial diln. of spinal fluid samples which have been previously coated on multiple wells of a microtiter plate. The P2 antibody bound to antigen on coated wells is further reacted with goat antirabbit IgG antibody linked to alk. phosphatase. The amt. of enzyme bound to the coatings is measured by reacting with a color generating substrate. The intensity of the color so formed gives an indication of the amt. of P2 protein in the spinal fluid samples. The invention includes an EIA kit consisting of antibody to P2 and other reagents necessary for the detn. High detectable amts. of P2 correlate with MS.
IC ICM G01N033-564
ICS G01N033-577
CC 9-10 (Biochemical Methods)
IT **Multiple sclerosis**
(diagnosis of, myelin P2 proteins immunochem. detn. in body fluid for)
IT **Immunochemical analysis**
(**enzyme-linked immunosorbent assay**, myelin P2 proteins detn. by, in body fluid, for demyelination detection)

IT **Proteins, specific or class**
RL: ANT (Analyte); ANST (Analytical study)
(**myelin basic**, P2, detn. of, immunochem., in body fluid, for demyelination detection)

L91 ANSWER 38 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 86226742 EMBASE
DN 1986226742
TI Serum and cerebrospinal fluid antibodies against myelin basic protein and their IgG subclass distribution in multiple sclerosis.
AU Garcia-Merino A.; Persson M.A.A.; Ernerudh J.; et al.
CS Department of Neurology, Karolinska Institutet, Huddinge University Hospital, Stockholm, Sweden
SO Journal of Neurology Neurosurgery and Psychiatry, (1986) 49/9 (1066-1070). CODEN: JNNPAU
CY United Kingdom
DT Journal
FS 008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
AB IgG class antibodies reactive with myelin basic protein (MBP) were determined by enzyme-linked immunosorbent assay (ELISA) in serum and cerebrospinal fluid (CSF) of 37 patients with multiple sclerosis and a control group of 32 patients with tension headache or psychoneurosis. Using standardised amounts of IgG from CSF and serum in ELISA, significantly higher mean antibody levels were found in CSF as well as in serum from the patients with multiple sclerosis. Ten (27%) of the multiple sclerosis CSF samples and 15 (41%) of the multiple sclerosis sera revealed anti MBP antibody levels exceeding 2 SD of the control group. Seven patients (19%) showed exclusive or higher levels of anti MBP antibodies in CSF, suggesting synthesis within the central nervous system. Analysis by ELISA for IgG subclasses of anti MBP antibodies revealed that they were restricted to IgG 1 in four patients and IgG 3 in one.
CT Medical Descriptors:
***multiple sclerosis**
cerebrospinal fluid
enzyme linked immunosorbent assay
serum
peripheral nervous system
priority journal
etiology
diagnosis
clinical article
human
central nervous system
blood and hemopoietic system
Drug Descriptors:
***autoantibody**
***immunoglobulin g**
***myelin basic protein**
RN (immunoglobulin g) 97794-27-9

L91 ANSWER 39 OF 39 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 86088946 EMBASE
DN 1986088946
TI Effect of methylprednisolone on CSF IgG parameters, myelin basic protein

and anti-myelin basic protein in multiple sclerosis exacerbations.
AU Warren K.G.; Catz I.; Jeffrey V.M.; Carroll D.J.
CS Department of Medicine, University of Alberta, Edmonton, Alta., Canada
SO Canadian Journal of Neurological Sciences, (1986) 13/1 (25-30).
CODEN: CJNSA2
CY Canada
DT Journal
FS 037 Drug Literature Index
008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
003 Endocrinology
030 Pharmacology
LA English
SL French
AB Clinical exacerbations of multiple sclerosis (MS) are characterized by elevated levels of cerebrospinal fluid (CSF) myelin basic protein (MBP). The purposes of this study were to determine whether anti-MBP antibodies are present in increased titer in CSF of MS patients with exacerbations, and whether they can be suppressed by the administration of immunosuppressive dosages of methylprednisolone (MP). A solid phase radio-immunoassay (RIA) was used to detect free and total anti-MBP antibodies before and after acid hydrolysis of CSF. In MS exacerbations, the majority of elevated anti-MBP is in the free form. With the exception of subacute sclerosing panencephalitis (SSPE) and some cases of post infectious encephalomyelitis, anti-MBP antibodies are not present in either MS patients in remission or in non-MS controls. Anti-MBP levels remained elevated over a 10 day period when patients are managed by bed rest only or when treated with intravenous (IV) ACTH. IV administration of MP in 'high' (160 mg/day) or 'mega' (2 g/day) dosages produces a highly significant reduction of both MBP ($p<0.01$) and anti-MBP ($p<0.001$) levels. Total intrathecal IgG synthesis is also significantly suppressed by IV-MP but not by ACTH.
CT Medical Descriptors:
*cerebrospinal fluid
*drug efficacy
*encephalitis
***multiple sclerosis**
*myelin basic protein antibody
*subacute sclerosing panencephalitis
exacerbation
radioimmunoassay
peripheral nervous system
priority journal
central nervous system
intravenous drug administration
oral drug administration
clinical article
diagnosis
therapy
human
Drug Descriptors:
***autoantibody**
*corticotropin
***immunoglobulin g**
*methylprednisolone
***myelin basic protein**
RN (corticotropin) 11136-52-0, 9002-60-2, 9061-27-2; (immunoglobulin g)

97794-27-9; (methylprednisolone) 6923-42-8, 83-43-2

NSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3

TI **Cationic antigens**. Problems associated with measurement by **ELISA**

AB The measurement of the mouse antibody response to cationized bovine serum albumin (cat BSA) and bovine gammaglobulin (cat BGG) was complicated because of the unique properties of these antigens. Cat BGG non-specifically bound rabbit anti-mouse gammaglobulin conjugated to alk. phosphatase. This was minimized by adding the polyanion, heparin. Cat BSA also reacted non-specifically with some conjugates, but the reaction with specific antibody was enhanced by the addn. of the polyanions heparin or dextran sulfate. The non-specific reaction did not appear to be related to the concn. of antigen used to coat the plastic plates. In addn., in **ELISA** inhibition expts. high concn. of antigens (>100 .mu.g/mL) seemed to result in non-specific inhibition of the antibody antigen reaction. A proposed model to explain the problems is based on the polycationic surface formed by coating the plates with the cationized proteins. This cationic surface can be neutralized by polyanions, reducing the non-specific and enhancing the specific reactions. It appears that other polycationic mols. might share these unique properties and these factors must be considered when they are measured.

SO Journal of Immunological Methods (1986), 87(1), 21-7
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AU Pesce, Amadeo J.; Apple, Raymond; Sawtell, Nancy; Michael, J. Gabriel

L6 ANSWER 28 OF 28 MEDLINE on STN DUPLICATE 10

TI Serum and cerebrospinal fluid antibodies against **myelin basic protein** and their IgG subclass distribution in **multiple sclerosis**.

AB IgG class antibodies reactive with **myelin basic protein** (MBP) were determined by enzyme-linked immunosorbent assay (**ELISA**) in serum and cerebrospinal fluid (CSF) of 37 patients with multiple sclerosis and a control group of 32 patients with tension headache or psychoneurosis. Using standardised amounts of IgG from CSF and serum in **ELISA**, significantly higher mean antibody levels were found in CSF as well as in serum from the patients with multiple sclerosis. Ten (27%) of the multiple sclerosis CSF samples and 15 (41%) of the multiple sclerosis sera revealed anti MBP antibody levels exceeding 2 SD of the control group. Seven patients (19%) showed exclusive or higher levels of anti MBP antibodies in CSF, suggesting synthesis within the central nervous system. Analysis by **ELISA** for IgG subclasses of anti MBP antibodies revealed that they were restricted to IgG 1 in four patients and IgG 3 in one.

SO JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY, (1986 Sep) 49 (9) 1066-70.
Journal code: 2985191R. ISSN: 0022-3050.

AU Garcia-Merino A; Persson M A; Ernerudh J; Diaz-Gil J J; Olsson T